Memo Dec. 12'68

Re: Dr Emile M. Scarpelli. The surfactant system of the lung. Leo Febiger Phila. 1968

Dear Mr. Holtzman: Enclosed are a few brief excerpts from this 275 page volume devoted to a discussion of present knowledge (clinical, pathological and experimental data) on the so called surfactant system of the lungs.

You may recall that I have promulgated in the literature of the past 35 yrs a concept of my own about the autonomic function of the pulmonary alveolar membrane which constitutes the surface between the air in the alveolar spaces and the pulmonary capillaries which brings the blood to the lungs for exchange of the gases. It is my concept that this surface is self producing and constantly recreates the extent and quality of the alveolar lining membrane in accordance with the needs of the body from moment to moment at rest and exercise. I described this surface as a "semifluid film" which is secreted by special cellular elements in the alveolar structures. It eventually turned out that this secretion contains substances which have marked surface tension reducing capacity enabling the airspaces resist contraction and deflation of the lungs. My theory of how this alveolar apparatus operates in visceral lung function was described in several papers which are in your file. The last one in the Lancet of Oct 1960 also describes the relationship of this to the origin and etiology of emphysema according to my concept.

In the literature of the last 20 yrs the surfactant function of the alveolar apparatus has been made the center of all attention. This literature is reviewed by Dr Scarpelli describing it under the title of The surfactant system of the lungs. In fact this is the "autonomous alveolar apparatus" which functions as the surface creating and maintaining organ in the lungs.

The book is too long and technical for you to go into at length but I thought you should know of it to the extent the above remarks the attached excerpts will afford.

JR.

(2)

Scarpelli. The surfactant system of the lung. Lea & Febiger Phila. '68.

p. 221 Cigarette smoke produces an acute increase in pulmonary resistance, probably secondary to bronchoconstriction and a fall in dynamic compliance. The change in compliance is probably due to uneven ventilation of alveoli rather than to decrease in the size or number of alveoli. These findings suggest that cigarette smoke does not alter surface tension properties of the lung. Therefore, the reportedly normal ~~[illegible]~~ γ_{min} (gamma min = minimal surface tension) and stability index of extracts from biopsy specimens from habitual cigarette smokers is not unexpected. However subsequent investigations demonstrated a significant reduction of surfactants in bronchial washings from chronic smokers without pulmonary symptoms. The relationship between smoke and surfactants may be more tenable than was first indicated.

A direct effect of cigarette smoke on extracts and bronchial washings from normal lungs of rats and dogs has been studied in vitro. Cigarette smoke significantly lowers the γ_{max} (maximal surface tension). This may be of significance to the development of emphysema in chronic smokers. The effect of cigarette smoke on γ_{min} (minimal surface tension) may vary. It reportedly lowers the min. surf. tension of extracts from rats lungs, whereas it reportedly increases the minimal surface tension of bronchial washings from lungs of dogs. The reasons for these apparently discordant findings are not known. There is some evidence that surface tension altering effects are due to particulate matter in the smoke; (1) house dust has similar effects and (2) these effects are abolished by filtration of the smoke. The latter indicates also that the chemical by-products of cigarette smoke may not affect surface tension. Filters of activated charcoal and cellulose acetate which do not remove particulate matter, are completely unavailing in preventing the deleterious effects of cigarette smoke on surfactants.

3

J + E M - Scarpelli Emphysema in rel. to alveo surf. tension

p 223 If the γ maximum of the alveolar lining membrane was lower than normal one would expect the alveoli to retain larger volumes than normal. Adult human lungs which retain larger volumes of air have the relatively lowest γ maximum (max. surface tension). Similarly they also have the lowest γ min (lowest tension surface) and highest stability index. These very stable lungs are there also hyperinflatable lungs. It is conceivable that low surface tension in adult lungs might produce a hyperinflatable state and that such a mechanism might be involved in the pathogenesis of emphysema. One study in which extracts from emphysematous lungs were compared with normal lungs demonstrated no significant differences between the two for γ min., dipalmityl lecithin phosphorus concentration, and palmitate concentration in lecithin. However there is much circumstantial evidence to warrant further investigation into the relationship between emphysema and lung surfactants, including the reported surface tension lowering effects of cigarette smoke, ~~air pollutants~~ sulfur dioxide, and aluminum oxide particles. Cigarette smoke and air pollutants are implicated strongly in the development of emphysema.

p 135 Other possible functions of the alveolar lining layer

One is tempted to imagine an autoregulatory mechanism in which normal surface tension insures normal geometry, liquid flux, surfactant flux and local perfusion. The latter in turn provides necessary metabolic precursors for the biosynthesis of the components of the lung surfactant system and the maintainance of normal surface tension.

Scarpelli: Surfactants as pollutants

S 231 The effect of pollutants such as particulate matter in cigarette smoke has been mentioned. The effect of sulfur dioxide on surface tension was studied in exposed rats. The findings suggested lowering of surface tension. The overall compliance of the exposed lungs was significantly higher than normal. The findings are similar to those reported for dust and cigarette particles in which surface tension of lung extracts esp γ max, was lowered by exposure to pollutants

Aluminum oxide particles also lower surface tension in rats exposed for 30 min-s and ozone produces a decrease in surface tension of lung extracts in vitro.

Low surface tension γmax (maximal surf. tension) may lead to a state of hyperinflatability of the lungs. Hyperinflatability may play a role in the pathogenesis of pulmonary emphysema as indicated before. The association between exposure to air pollutants such as particulate matter and sulfur dioxide, and the lowering of pulm. surface tension seems well established. The relationship between low surf. tension and hyperinflatability and thus pulmonary emphysema seems too strong to be overlooked.